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TI Diterpenoids from the roots of *Salvia sclarea*.
AU Ulubelen, Ayhan (1); Sonmez, Ufuk (1); Topcu, Gulacti
CS (1) Fac. Pharm., Univ. Istanbul, 34452 Istanbul Turkey
SO Phytochemistry (Oxford), (1997) Vol. 44, No. 7, pp. 1297-1299.
ISSN: 0031-9422.
DT Article
LA English

TI 2-BETA HYDROXYHAUTRIWAIC-ACID A CLERODANE TYPE DITERPENOID AND OTHER
TERPENOID FROM THREE BACCHARIS SPECIES.
AU ARRIAGA-GINER F J; WOLLENWEBER E; SCHOBER I; DOSTAL P; BRAUN S
CS DEPARTAMENTO DE QUIMICA ORGANICA, UNIVERSIDAD AUTONOMA DE MADRID,
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BLANCO, E-28034 MADRID, SPAIN.
SO PHYTOCHEMISTRY (OXF), (1986) 25 (3), 719-722.
CODEN: PYTCAS. ISSN: 0031-9422.
FS BA; OLD
LA English

TI Diterpenes from the genus *Amaracus*
AU Passannanti, Salvatore; Paternostro, Mariapia; Piozzi, Franco; Barbagallo,
Claudia
CS Inst. Org. Chem., Univ. Palermo, Palermo, Italy
SO Journal of Natural Products (1984), 47(5), 885-9
CODEN: JNPRDF; ISSN: 0163-3864
DT Journal
LA English

TI A DITERPENE AND FLAVONOID OF BACCHARIS-FLABELLATA.
AU SAAD J R; DAVICINO J G; GIORDANO O S
CS DEPARTAMENTO DE QUIMICA ORGANICA, FAC. DE QUIMICA BIOQUIMICA Y FARMACIA,
UNIVERSIDAD NACIONAL DE AN LUIS CHACABUCO Y PEDERNERA, 5700 SAN LUIS,
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SO PHYTOCHEMISTRY (OXF), (1988) 27 (6), 1884-1887.
CODEN: PYTCAS. ISSN: 0031-9422.
FS BA; OLD



DITERPENOIDS FROM THE ROOTS OF *SALVIA SCLAREA*

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Key Word Index—*Salvia sclarea*; Lamiaceae; triterpenoids; steroid; diterpenoids; sclareapinone; acetylsalvipisone.

Abstract—The roots of *Salvia sclarea* yielded two triterpenoids, 3-oxo-oleanolic acid, α -amyrin, a steroid sitosterol and 12 diterpenoids, two of which are new. The known diterpenoids are ferruginol, salvipisone, microstegiol, candidissiol, 2,3-dehydrosalvipisone, aethiopione, 1-oxo-aethiopione, salvinolone, cryptojaponol, Δ^7 -manool, and the new compounds are sclareapinone and acetylsalvipisone. The structures were established by spectral data and also by TLC comparison for the known compounds. Copyright © 1997 Elsevier Science Ltd

INTRODUCTION

In a previous study with the whole plant of *Salvia sclarea* L. collected from central Turkey (Sivas), we isolated seven known and two new diterpenoids, together with sesquiterpenes and flavones [1]. In the present study with the roots of the same plant collected from a different location of central Turkey (Çorum), two triterpenoids, 3-oxo-oleanolic acid, α -amyrin and sitosterol as well as 12 diterpenoids were isolated. Five of the diterpenoids, ferruginol [2], salvipisone [3], microstegiol [4], candidissiol [5], 2,3-dehydrosalvipisone [1], were isolated from both collections, while the others, sclareol [6], manool [7], 7-oxoroyleanone [8] and 7-oxoferruginol-18-al [1], were only found in the first study. However, additional diterpenoids cryptojaponol [9], aethiopione [10], 1-oxo-aethiopione [11], salvinolone [12], Δ^7 -manool [13] as well as new diterpenoids sclareapinone (1) and acetylsalvipisone (2) were isolated in the present study. Sclareol is an important bioactive diterpene [14, 15], but it was not found in this collection; however, its dehydroxylated derivative Δ^7 -manool was present. The structures of the known compounds were established by comparing their spectral data with literature values and by TLC comparison with authentic samples, except for Δ^7 -manool. There is only one other study with *S. sclarea*, by a Russian group [16]; they have found tanshinone, isotanshinone, hydroxytanshinone, which were not present in the Turkish collections of the plant.

RESULTS AND DISCUSSION

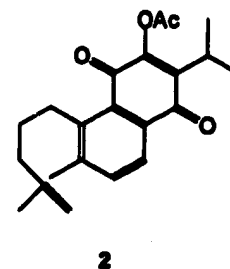
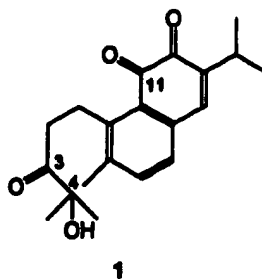
The new diterpene sclareapinone (1) had a molecular formula $C_{20}H_{24}O_4$ as deduced from its HREI mass

spectrum (m/z 328.1698, calc. 328.1674). The IR spectrum exhibited frequencies for a hydroxyl at 3400 cm^{-1} , an oxo group at 1725 cm^{-1} and an orthoquinoid group at 1680 , 1640 and 1605 cm^{-1} , together with UV maxima at 432 (sh), 390, 332 nm, indicating an aethiopione derivative for 1. The ^1H NMR spectrum corroborated this suggestion with the signals at δ 7.06 (1H, d , $J = 8\text{ Hz}$, H-7), 6.95 (1H, d , $J = 8\text{ Hz}$, H-6), 6.80 (1H, d , $J = 1\text{ Hz}$, H-14), 2.90 (1H, d septet, $J = 1$ and 7 Hz , H-15), 2.25 (3H, s , Me-20), 1.45 and 1.38 (each 3H, s) (Me-18 and Me-19), 1.17 (3H, d , $J = 7\text{ Hz}$), 1.13 (3H, d , $J = 7\text{ Hz}$) (Me-16 and Me-17). Spin decoupling experiments showed the relations between C-1 and C-2 protons at δ 2.85 (1H, m , H-1 β), 2.58 (1H, m , H-2 α), 2.42 (1H, ddd , $J = 4, 7$ and 1 Hz , H-2 β) and 2.0 (1H, m , H-1 α). The chemical shifts of the two methyl groups (Me-18 and Me-19) as well as the lack of an isopropyl methine proton (H-4) suggested the presence of a hydroxyl group at C-4. The oxo group could be placed at C-1, C-2 or C-3, its being at C-2 was unlikely due to the absence of the signals for the isolated methylene groups in its ^1H NMR spectrum. As for C-1 and C-3 positions, the latter was evident from the mass degradation of the side chain, at m/z 268 $[\text{M} - \text{C}_3\text{H}_5\text{O} + \text{H}]^+$ (22%); 241 $[\text{M} - \text{C}_4\text{H}_7\text{O}_2]^+$ (40%), 227 $[\text{M} - \text{C}_5\text{H}_9\text{O}_2]^+$ (90%) and 213 $[\text{M} - \text{C}_6\text{H}_{11}\text{O}_2]^+$ (48%). The ^{13}C NMR spectrum supported the placement of the oxo group as well as the given structure (Table 1). Thus, 1 is 3-oxo-4-hydroxyaethiopione and is named sclareapinone.

The second new compound was the acetyl derivative of salvipisone (2). Salvipisone was isolated in previous [1] and present studies of *S. sclarea* as well as from *S. candidissima* subsp. *occidentalis* [17]. A literature

Table 1. ^{13}C NMR data for compounds 1 and 2

C	1	2
1	28.9 t	27.1 t
2	36.0 t	30.0 t
3	210.7 s	38.4 t
4	74.2 s	145.6 s
5	139.9 s	142.0 s
6	136.4 d	136.6 d
7	128.0 d	126.5 d
8	134.6 s	133.5 s
9	134.8 s	126.5 s
10	144.6 s	144.7 s
11	181.2 s	183.3 s
12	182.3 s	150.0 s
13	148.4 s	123.8 s
14	140.0 d	184.5 s
15	26.8 d	24.6 s
16	21.4 q	20.0 q
17	20.9 q	20.3 q
18	22.3 q	110.2 t
19	26.4 q	22.6 q
20	19.8 q	20.2 q
C=O	—	164.6 s
Me	—	21.1 q



survey revealed that there is no acetylsalvipisone occurring naturally. Compound 2 could be an artefact although we did not use any drastic acetylating agent; only ethyl acetate was used for the elution of the column. Nevertheless, the spectroscopic data for 2 is as follows. The HREI mass spectrum of 2 indicated a molecular formula $\text{C}_{22}\text{H}_{34}\text{O}_4$ (m/z : 354.3822; calc. 354.3831). The ^1H NMR signals were quite similar to those of salvipisone at δ 7.90 (1H, d, J = 8 Hz, H-7), 7.49 (1H, d, J = 8 Hz, H-6), 4.80 (2H, br s, CH₂-18), 3.37 (1H, septet, J = 7 Hz, H-15), 2.43 (3H, s, Me-20), 2.05 (3H, s, OAc), 1.80 (3H, s, Me-19), 0.98 and 1.00 (each 3H, d, J = 7 Hz) (Me-16 and Me-17). The main difference between salvipisone and acetylsalvipisone was the observation of the presence of an acetyl group at δ 2.05 and the chemical shift of the two methyl doublets upfield compared to salvipisone. Hydrolysis of the acetyl group using 5% NaOH yielded salvipisone (TLC comparison), thus verifying the structure of 2. The ^{13}C NMR spectrum of 2 correlated with the given structure (Table 1).

EXPERIMENTAL

General. UV: in MeOH; IR: in CHCl_3 ; ^1H and ^{13}C NMR in CDCl_3 ; HRMS: VG ZabSpec; Chromatotron Model 7924 T.

Plant material. Roots of *S. sclareu* were collected from central Turkey (Alacahöyük-Sungurlu, Çorum) and identified by Prof. Dr N. Özhatay. A voucher specimen (ISTE 68381) is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul.

Extraction and isolation. Dried roots of the plant (630 g) were extracted with distilled Me_2CO in a Soxhlet apparatus; the solvent was evaporated *in vacuo*, and 12 g residue was obtained and fractionated on a silica gel column (5 × 70 cm) using PE; a gradient of EtOAc was added up to 100%, followed by EtOH. The combined fractions were further separated on a Chromatotron using silica gel plates. When necessary prep. TLC plates were used to obtain pure compounds. The following compounds were isolated: 1 (15 mg), ferruginol (12 mg), Δ^7 -manool (9 mg), microstegiol (15 mg), candidissol (8 mg), 2 (12 mg), salvipisone (10 mg), 2,3-dehydrosalvipisone (15 mg), salvinolone (8 mg), aethiopinone (10 mg), 1-oxoaethiopinone (15 mg), cryptojaponol (20 mg), α -amyrin (18 mg), 3-oxo-oleanolic acid (10 mg) and sitosterol (25 mg).

Sclareapinone (1). Amorphous orange compound. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 432 (sh), 390 (2.0), 332 (3.1), 230 (4.2). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3400, 2960, 2920, 2860, 1725, 1680, 1640, 1605, 1460, 1380, 1280, 1160, 1120, 1090, 1030. ^1H NMR (CDCl_3) given in text; ^{13}C NMR (CDCl_3): Table 1. HREIMS m/z (percent): 328.1698 [M]⁺ (5), 310 [M - H₂O]⁺ (15), 286 [M - C₂H₅]⁺ (39), 268 [M - C₂H₅O + H]⁺ (22), 241 [M - C₂H₅O]⁺ (40), 227 [M - C₂H₅O]⁺ (90), 213 [M - C₂H₅O]⁺ (48), 173 (24), 128 (25), 78 (28), 69 (31).

Acetylsalvipisone (2). Amorphous orange compound. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 425 (2.4), 360 (3.5), 280 (4.0), 245 (4.2). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3050, 3020, 2980, 2850, 1725, 1680, 1665, 1650, 1590, 1560, 1475, 1380, 1250, 1230, 1100, 980. ^1H NMR (CDCl_3) given in text; ^{13}C NMR (CDCl_3): Table 1. HREIMS m/z (percent): 354.3822 [M]⁺ (18), 312 [M - Ac + H]⁺ (100), 296 [M - HOAc]⁺ (45), 271 [M - C₂H₅]⁺ (20), 243 (15), 186 (8), 97 (12), 69 (75).

Hydrolysis of compound 2. To a solution of 2 (5 mg) in MeOH, 2 ml 5% NaOH was added and refluxed for 2 hr. Deacetylated 2 was extracted with CHCl_3 and compared with authentic salvipisone on TLC plates; their ^1H NMR spectra were found to be identical.

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